COMPLETE LISTING OF CLAIMS
IN ASCENDING ORDER WITH STATUS INDICATOR

1. (Canceled)

2. (Currently amended) A method for identifying the sequence of a portion of sample DNA comprising the steps of:

(i) forming immobilised double stranded DNA comprising one strand of sample DNA and one strand of primer DNA on one or more reaction areas in a microchannel structure of a microfluidic device, ~~DNA primers of said one or more reaction areas are hybridised to said sample DNA~~;

(ii) adding a deoxynucleotide, deoxynucleotide analogue or dideoxynucleotide and a DNA polymerase to each of said one or more reaction areas so that extension of primer occurs as a result from complementarity of the added deoxynucleotide, deoxynucleotide analogue or dideoxynucleotide with the strand of sample DNA that is part of the immobilised double stranded DNA;

(iii) detecting whether or not the deoxynucleotide, deoxynucleotide analogue or dideoxynucleotide added in step (ii) is added to the primer DNA in said one or more reaction areas;

(iv) removing pyrophosphate, DNA polymerase or the excess of deoxynucleotide, deoxynucleotide analogue, or dideoxynucleotide from one or more reaction areas;

(~~i~~v) repeating steps (ii) – (iv~~iii~~) with different deoxynucleotides, deoxynucleotide analogues or dideoxynucleotides ~~the required number of times for the identification of said sequence~~; and

(vi) identifying said sequence from the results of ~~step (iiiv)~~the above previous steps.

3. (Canceled)

4. (Currently Amended) A method for identifying the sequence of a portion of sample DNA, comprising the steps of:

(i) adding sample DNA to ~~a predetermined area on~~ a microfluidic device;

(ii) moving the sample DNA to a reaction chamber on the microfluidic device;

(iii) attaching the sample DNA to a surface of the reaction chamber, wherein a DNA primer is hybridised to the sample DNA in a single stranded form, ~~or hybridising the sample DNA in single stranded form to a DNA primer that is attached to the surface of the reaction chamber~~

(iv) adding a deoxynucleotide, deoxynucleotide analogue or dideoxynucleotide and a DNA polymerase to said reaction chambers so that extension of primer DNA occurs as a result from complementarity of the added deoxynucleotide, deoxynucleotide analogue or dideoxynucleotide with the strand of sample DNA that is attached to the surface of the reaction chamber;

(v) detecting whether or not the deoxynucleotide, deoxynucleotide analogue or dideoxynucleotide added in step (iv) is added to the primer DNA in said reaction chamber;

(vi) removing pyrophosphate, DNA polymerase or the excess of deoxynucleotide, deoxynucleotide analogue, or dideoxynucleotide from one or more reaction areas;

(vii) repeating steps (iv) – (vi) with different deoxynucleotides, deoxynucleotide analogues or dideoxynucleotides; and

(viii) identifying said sequence from the results of ~~step (vii)~~of the above previous steps.

~~(iv) extending the primer in the presence of a DNA polymerase with a deoxynucleotide, deoxynucleotide analogue, or dideoxynucleotide, wherein~~

~~the extension is indicated by release of pyrophsophate from the extension reaction;~~

~~(v) repeating step (iv) the required number of times for the identification of said sequence; and~~

~~(vi) identifying said sequence from the deoxynucleotides, deoxynucleotide analogues, or dideoxynucleotides that resulted in primer extension in step (iv).~~

5. (Canceled)

6. (Currently amended) The method of claim 2, wherein ~~a~~ the deoxynucleotide, deoxynucleotide analogue, or dideoxynucleotide ~~which is labelled~~that is added in step (ii) is labelled.

7. (Canceled)

8. (Canceled)

9. (Canceled)

10. (Canceled)

11. (Canceled)

12. (Currently amended) The method of claim 2, wherein the microfluidic device is a disc and the fluids are moved by ~~centripetal~~ centrifugal force within the microfluidic device.

13. (Canceled)

14. (Canceled)

15. (Canceled)

16. (Currently amended) The method of claim 4, wherein the microfluidic device is a disc and the fluids are moved by ~~centripetal~~ centrifugal force within the microfluidic device.

17. (Canceled)

18. (Canceled)

19. (New) A method for identifying the sequence of a portion of sample DNA, comprising the steps of:

i) attaching at least one primer DNA to each of between one and 100,000 areas to the surface within a reaction chamber of a microfluidic device;

(ii) adding sample DNA to the microfluidic device;

(iii) moving the sample DNA to the reaction chamber on the microfluidic device;

(iv) hybridising the sample DNA in single stranded form to the primer DNA;

(v) adding a deoxynucleotide, deoxynucleotide analogue or dideoxynucleotide and a DNA polymerase to the reaction chamber so that extension of primer DNA occurs as a result from complementarity of the added deoxynucleotide, deoxynucleotide analogue or dideoxynucleotide with the strand of sample DNA;

(vi) detecting whether or not the deoxynucleotide, deoxynucleotide analogue or dideoxynucleotide added in step (v) is added to the primer DNA in said reaction chamber;

(vii) removing pyrophosphate, DNA polymerase or the excess of deoxynucleotide, deoxynucleotide analogue, or dideoxynucleotide from one or more reaction areas;

(viii) repeating steps (v) – (vii) with different deoxynucleotides, deoxynucleotide analogues or dideoxynucleotides; and

(ix) identifying said sequence from the results of the above previous steps.

20. (New) The method of claim 2, wherein the detecting step (iii) measures the release of pyrophosphate.

21. (New) The method of claim 20, wherein the pyrophosphate release is detected by light emitted from a luciferin luciferase reaction.

22. (New) The method of claim 6, wherein the label is a fluorescent label.

23. (New) The method of claim 4, wherein the detecting step (v) measures the release of pyrophosphate.

24. (New) The method of claim 23, wherein the pyrophosphate release is detected by light emitted from a luciferin luciferase reaction.

25. (New) The method of claim 4, wherein the deoxynucleotide, deoxynucleotide analogue, or dideoxynucleotide that is added in step (iv) is labelled.

26. (New) The method of claim 25, wherein the label is a fluorescent label.

27. (New) The method of claim 19, wherein the detecting step (vi) measures the release of pyrophosphate.

28. (New) The method of claim 27, wherein the pyrophosphate release is detected by light emitted from a luciferin luciferase reaction.

29. (New) The method of claim 19, wherein the deoxynucleotide, deoxynucleotide analogue, or dideoxynucleotide that is added in step (v) is labelled.

30. (New) The method of claim 28, wherein the label is a fluorescent label.

31. (New) The method of claim 19, wherein the microfluidic device is a disc and the fluids are moved by centripetal force.

REMARKS/ARGUMENTS

Claims 1-18 are pending in the present application. Claims 2, 4, 6, 12 and 16 have been amended without prejudice and without acquiescence. Claims 1, 3, 5, 7-11, 13-15 and 17-18 have been canceled without prejudice and without acquiescence. Claims 19-31 have been added. Support for claims 19-31 can be found throughout the specification and the original and/or canceled claims. No new matter has been added.

The issues outstanding in this application are as follows:

- Claims 1-17 were rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite.

- Claims 1, 3, 5, 7, 9, 13 and 17 were rejected under 35 U.S.C. § 102(b) as being anticipated by Ronaghi et al. (Anal. Biochemistry, 1996).

- Claims 1-18 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Ronaghi et al., in view of Mian et al., (US 6,319,469).

Applicants respectfully traverse the outstanding rejections, and Applicants respectfully request reconsideration and withdrawal thereof in light of the amendments and remarks contained herein.

I. 35 U.S.C. § 112, second paragraph rejection

Claims 1-17 are rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. Applicants respectfully traverse.

A. Claims 1, 5, 7, and 8.

Claims 1, 5, 7, and 8 are rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. Applicants respectfully traverse.

In order to advance the prosecution of the present application, Applicants have canceled claims 1, 5, 7 and 8 without prejudice and without acquiescence. Thus, in light of these amendments, the rejection is moot and Applicants respectfully request that the rejection be withdrawn.

B. Claims 2-4, 6, 9, 10, 13-17.

Claims 2-4, 6, 9, 10, 13-17 are rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. Applicants respectfully traverse.

In order to advance the prosecution of the present application, Applicants have amended independent claims 2 and 4 without prejudice and without acquiescence to clarify the scope of the present invention and have canceled claims 3, 9, 10, 13, 14, 15, and 17 without prejudice and without acquiescence. Thus, in light of these amendments, Applicants respectfully request that the rejection be withdrawn.

C. Claims 3, 9, 13, 14 and 17.

Claims 3, 9, 13, 14 and 17 are rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. Applicants respectfully traverse.

In order to advance the prosecution of the present application, Applicants have canceled claims 3, 9, 13, 14 and 17 without prejudice and without acquiescence. Thus, in light of these amendments, the rejection is moot and Applicants respectfully request that the rejection be withdrawn.

D. Claims 2, 4, 6, 10, 11, 12, 15, and 16.

Claims 2, 4, 6, 10, 11, 12, 15, and 16 are rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. Applicants respectfully traverse.

In order to advance the prosecution of the present application, Applicants have amended independent claims 2 and 4 to clarify the scope of the claims without prejudice and without acquiescence and have canceled claims 10, 11, and 15 without prejudice and without acquiescence. Thus, in light of these amendments, the rejection is moot and Applicants respectfully request that the rejection be withdrawn.

II. 35 U.S.C. § 102(b)

Claims 1, 3, 5, 7, 9, 13 and 17 are rejected under 35 U.S.C. § 102(b) as being anticipated by Ronaghi et al. (Anal. Biochemistry, 1996). The Action states that Ronaghi et al. teaches the methods of using a microfluidic device to determine a nucleotide base in a nucleic acid sample. Applicants respectfully traverse.

In order to advance the prosecution of the present application, Applicants have canceled claims 1, 3, 5, 7, 9, 13 and 17 without prejudice and without acquiescence. Thus, in light of these amendments, the rejection is moot and Applicants respectfully request that the rejections be withdrawn.

III. 35 U.S.C. § 103(a)

Claims 1-18 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Ronaghi et al. in view of Mian et al., (US 6,319,469). The Action states that Ronaghi et al. teaches a method of identifying a sequence of a portion of DNA, but does not teach identifying a sequence of a portion of DNA using a microfluidic device. The Action further states that Mian et al. teaches the use of a microfluidic device for the method of Ronaghi et al. Applicants respectfully traverse.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka,* 490 F.2d 981, 180 USPQ 580 (CCPA 1974).

The microfluidic device of the present invention is utilized such that the excess reagents and soluble products are easily removed/separated from a growing immobilized primer to decrease the risk of artifacts. Applicants assert that neither Ronaghi et al. nor Mian et al. teach and/or suggest removing excess reagents during their sequencing reactions.

In order to advance the prosecution of this application, Applicants have amended independent claims 2 and 4 without prejudice or without acquiescence. The addition of the removing step to independent claims 2 and 4 makes the subject matter of claims 2 and 4 non-obvious over Ronaghi et al. in view of Mian et al. since neither reference teaches and/or suggest the removal of excess reagents (such as deoxynucleotides, deoxynucleotide analogues, dideoxynucleotide, pyrophosphate or DNA polymerase) during the sequencing reaction.

Regarding dependent claims 6, 12, 16, if an independent claim is non-obvious under 35 U.S.C. 103(a), then any claim depending therefrom is by definition non-obvious. *In re Fine*, 5 USPQ 2d 2596 (Fed. Cir. 1988). Dependent claims 6, 12, 16 depend from amended independent claim 2 or 4 and, thus contain all the limitations of the independent claims and are non-obvious. For the same reason, Applicant respectfully submits that new dependent claims 20-26 are also allowable.

Accordingly, Applicant respectfully submits reconsideration and withdrawal of the outstanding rejection under 35 U.S. C. 103(a) as being unpatentable over Ronaghi et al. in view of Mian et al.

CONCLUSION

Claims 1-18 are pending in the present application. Claims 2, 4, 6, 12 and 16 have been amended without prejudice and without acquiescence. Claims 1, 3, 5, 7-11, 13-15 and 17-18 have been canceled without prejudice and without acquiescence. Claims 19-31 have been added. No new matter has been added.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 06-2375, under Order No. 10104789 from which the undersigned is authorized to draw.

Dated: July 17, 2003

Respectfully submitted,

By _____

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